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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Hiroyuki Hashimoto

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EXAMINER

STRZELECKA, TERESA E

ART UNIT

PAPER NUMBER

1637

MAIL DATE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/519,813	Applicant(s) HASHIMOTO ET AL.	
	Examiner TERESA E. STRZELECKA	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-56 is/are pending in the application.
- 4a) Of the above claim(s) 4,6,9,10,13,14,16-29,32,34,37,38,41,43 and 48-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,7,8,11,12,15,30,31,33,35,36,39,40,42 and 44-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/27/09;4/28/09;5/22/09</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. This office action is in response to an amendment filed April 28, 2009. Claims 1-56 were previously pending, with claims 4, 6, 9, 10, 13, 14, 16-29, 32, 34, 37, 38, 41, 43 and 48-56 withdrawn from consideration. Applicants amended claims 1, 2, 15 and 39. Claims 1-3, 5, 7, 8, 11, 12, 15, 30, 31, 33, 35, 36, 39, 40, 42 and 44-47 will be examined.
2. Applicants' amendments overcame all of the previously presented rejections. This office action contains new grounds for rejection necessitated by amendment.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on March 27, 2009 and April 28, 2009 were filed after the mailing date of the non-final office action on February 2, 2009. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.
4. The information disclosure statement (IDS) submitted on May 22, 2009 was filed after the mailing date of the non-final office action on February 2, 2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, the references will not be printed, since this IDS is the duplicate of one filed on April 28, 2009.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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6. Claims 1-3, 5, 7, 8, 11, 12, 15, 30, 31, 33, 35, 36, 39, 40, 42 and 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okamoto et al. (Nature Biotechnol., vol. 18, pp. 438-441, 2000; cited in the IDS and in the previous office action), Park (U.S. Patent No. 6,839,454 B1; cited in the previous office action), Rava et al. (WO 99/39817; cited in the IDS and in the previous office action), Sundberg et al. (U.S. Patent No. 5,624,711 A), Strother et al. (U.S. Patent No. 6,569,979 B1), Corn et al. (U.S. Patent No. 6,127,129 A) and Maxim et al. (U.S. Patent No. 7,191,901 B2).

Claims 1, 2, 11, 12, 15, 30, 39, 46 and 47 will be considered together in claim 2, since it is a species of claims 1, 11, 12, 15, 30, 39, 46 and 47.

A) Regarding claims 1, 2, 11, 12, 15, 30, 39, 46 and 47, Okamoto et al. teach a method comprising:

- (a) a step of designing plural kinds of probes for detecting a target substance (Fig. 4);
- (b) a step of synthesizing the designed plural probes (page 440, second paragraph; page 441, second paragraph; Okamoto et al. do not specifically teach synthesizing the probes, but since they had them, they inherently had to be synthesized.);
- (c) a step of individually purifying the synthesized plural probes (page 440, second paragraph; page 441, second paragraph; Okamoto et al. do not specifically teach purifying the probes, but since they had them, they inherently had to be synthesized and purified after synthesis.);
- (d) a step of obtaining probe information on each purified probe (page 440, second paragraph; page 441, second paragraph; Okamoto et al. do not specifically teach obtaining probe information, but since they had them, they inherently had to be synthesized and purified after synthesis, therefore, they knew they had purified probes, i.e., obtained information about the probes.);

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(e) a step of judging "good" or "not good" state of synthesis and purification in each purified probe according to the obtained probe information and a predetermined criterion (page 440, second paragraph; page 441, first and second paragraph; page 438, 7th paragraph; Fig. 2; where the probes' integrity was determined using HPLC after deposition onto a surface);

(f) a step of repeating the foregoing steps (b) to (e) on the purified probe of which state of synthesis and purification is judged as "not good", thereby obtaining "good" state of synthesis and purification in all the purified probes Okamoto et al. teach repeating the steps with different probes (page 440, second paragraph; page 441, first and second paragraph; page 438, 7th paragraph; Fig. 2).);

(g) a step of individually dissolving each purified probe judged as "good" in a solvent for ejection to a carrier, based on at least a part of the probe information obtained in (d), in a predetermined concentration and storing each obtained probe solution in an individual storing container (page 438, paragraphs 6 and 7; page 439, second paragraph);

(h) a step of transferring each probe solution stored in the storing container to another container equipped in an apparatus for deposition onto the carrier (page 438, 7th paragraph; page 439, second paragraph; inherent in the fact that dissolution was not done in the ink-jet printer);

(i) a step of applying a surface treatment for fixing the probe to the carrier (page 438, last paragraph; page 439, first paragraph; page 441, fourth paragraph);

(j) a step of depositing the probe solution onto a treated surface of the carrier by a method including following steps, thereby forming a plurality of mutually independent probe fixation areas;

(j-2) a step of depositing at least one selected from plural probe solutions onto the carrier judged as "good" so as to form a probe deposition area independent for each probe solution (page 439, second and third paragraphs);

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(j-3) a step of executing an inspection, concerning a formed state of the probe deposition area, on the carrier on which the probe deposition area is formed, and judging "good" or "not good" state of the deposition according the result of the inspection and a predetermined criterion (page 439, paragraphs 4, 7; Fig. 3; where the spot distribution and shape were examined);

(j-4) a step of executing, on the carrier having the probe deposition area judged as "good", a fixation of the probe to the surface of the carrier thereby obtaining a probe carrier (page 439, second and third paragraphs);

(j-5) a step of executing an analytical inspection on the probe in at least one of the plural probe fixation areas constituted of probes fixed on the carrier; and (j-6) a step of judging "good" or "not good" state of the produced probe carrier according to the result of the analytical inspection and a predetermined criterion (page 439, paragraphs 4, 7; Fig. 3; where the spot distribution and shape were examined, also Fig. 5 and 6, where the hybridization reactions to proper probes were examined).

Regarding claims 3, 31 and 40, Okamoto et al. teach nucleic acid probes (page 440, second paragraph; Fig.4).

Regarding claims 5, 33 and 42, Okamoto et al. teach detecting purity of nucleic acid probes (page 440, second paragraph; page 441, first and second paragraphs).

Regarding claims 7, 35 and 44, Okamoto et al. teach covalent bonding of nucleic acid probes (page 438, last paragraph; page 439, first paragraph).

Regarding claims 8, 36 and 45, Okamoto et al. teach inkjet apparatus with single and plural ink jet nozzles (page 439, paragraphs 2 and 8).

B) Regarding step (j-1), Okamoto et al. do not teach inspecting the carrier after the surface treatment.

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C) Regarding claims 1, 2, 11, 12, 15, 30, 39, 46 and 47, Rava et al. teach quality control process for manufacturing biochips (page 1, lines 1-16; page 6, lines 6-18; page 14, lines 12-23; page 15, lines 1-2). Rava et al. specifically teach that each of the steps of array manufacturing can be subject to a quality control before further processing (page 17, lines 5-8) and testing of substrates after they were coated with xilane but before attachment of oligonucleotides (page 17, lines 9-14).

D) Park specifically teaches quality control analysis of fabricated DNA microarrays (Fig. 3, 5; col. 17, lines 33-67; col. 18-20), where the following parameters are analyzed: signal area (col. 17, lines 55-67; col. 18, lines 1-4), spot area (col. 18, lines 5-30), degree of ellipticity (col. 18, lines 31-58), square perimeter-to-spot area ratio (col. 18, lines 59-67; col. 19, lines 1-5); difference in the intensity of contamination regions versus signal region (col. 19, lines 6-13); deviation of spot's center location from canonical location (col. 19, lines 14-28), degree of alignment between sub-grids (col. 19, lines 29-54), uniformity in the distance between sub-grids (col. 19, lines 55-67 and col. 20, lines 1-12), variation in the identified background (col. 20, lines 13-34), determination of missing sub-grids (col. 20, lines 35-42) and parallelism of rows and columns (col. 20, lines 43-56).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the methods of quality control of Park and Rava et al. in the chip production process of Okamoto et al. The motivation to do so is provided by Rava et al. (page 1, lines 6-13):

“Typically, the quality control testing of the items to be manufactured is performed at the point the item of manufacture is completed. In the event that the representative sample of items fails the requisite standards, all the items that had been processed with samples which would be expected to have similar defects are rejected. When the basis for rejection exists because of a process which occurred several steps prior to the completion of the product, the further processes were performed unnecessarily, at a great expense of time and money.”

E) None of the above references teach examining the surface of the carrier using contact angle measurement. However, as can be seen from the references cited below, contact angle measurement was commonly used in the art to determine quality of derivatized surfaces and their properties.

F) Sundberg et al. teach derivatization of solid supports used in the solid-phase synthesis of oligonucleotide or peptide arrays (Abstract). They teach that the following factors determine the quality of oligomer arrays: spacing of synthesis initiation sites, wettability of the surface and non-specific binding of ligands and the ways in which these parameters affect the hybridization experiments (col. 10, lines 1-54). They teach using different functional groups for derivatization of the substrates and characterization of the derivatized surfaces using contact angle measurement (Fig. 2; Fig. 14; col. 5, lines 25-35; col. 20, lines 7-44). Example 2 (col. 20, lines 52-67, col. 21, lines 1-35) describes determination of density of functional groups on the surface using fluorescent labels, whereas col. 21, lines 37-59 describe determination of chemical coupling efficiency.

The wettability of surfaces created with different functional groups by contact angle measurement is described in col. 20, lines 60-67 and col. 21. Finally, the quality determination of the final product is determined using an assay which determines a degree of non-specific-binding to the array surface (col. 23, lines 1-60).

G) Strother et al. teach creation of derivatized surfaces in order to create molecular arrays (Abstract). They teach derivatization of unoxidized carbon, silicon and germanium substrates with ω -modified alkenes and further attachment of oligonucleotides to such surfaces (col. 5, lines 45-67; col. 6; col. 7, lines 1-62). They teach quality control of every step of the surface derivatization process (col. 8, lines 1-64), where contact angle measurements were performed to determine the extent of deprotection of the surface (col. 8, lines 46-64).

Strother et al. also teach quality control characterization of the surfaces finally derivatized with nucleic acids: detection of hybridization specificity (col. 8, lines 65-67; col. 9, lines 1-15), surface density of attachment sites (col. 9, lines 16-67) and stability under conditions of repeated hybridization (col. 9, lines 65-67; col. 10, lines 1-27).

H) Corn et al. teach a method of producing biomolecular arrays on metal surfaces (Abstract) in a process outlined in Fig. 1 and described in col. 3, lines 15-67; col. 4, lines 1-64; col. 6, lines 49-67; col. 7-9; and col. 10-lines 1-39). Corn et al. teach the following tests of the quality of surfaces:

i) after step (1), detection of a PM-FTIRRAS spectra (col. 11, lines 52-63; Fig. 3A) to determine the degree of amino group protonation and measurement of contact angle to determine the degree of surface hydrophobicity (col. 11, lines 64-67; col. 12, lines 1-6; col. 7, lines 36-60);

ii) after step (2), again detection of a PM-FTIRRAS spectra (Fig. 3B) to determine the degree of amino group protection and measurement of contact angle to determine the degree of surface hydrophobicity (col. 8, lines 15-37);

iii) after step (6), detection of a PM-FTIRRAS spectra (Fig. 3C) to determine the degree of protecting group removal (col. 9, lines 51-61);

iv) after step (7), detection of the degree of binding of PEG-NHS groups to deprotected amino groups using PM-FTIRRAS spectra (Fig. 3D) and measurement of contact angle to determine the degree of surface hydrophilicity, as well as measurement of a thickness of the derivatized film (col. 10, lines 8-34) and the degree of non-specific binding (col. 10, lines 35-39).

I) Maxim et al. used measurement of contact angle and background fluorescence to examine the influence of materials used as storage containers on the properties of derivatized surfaces used to make biomolecular arrays (col. 1, lines 43-58; col. 6, lines 20-49; Table I; col. 7, lines 29-67; col. 8, lines 29-40; Fig. 2 and 3).

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Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the measurement of contact angle as described by Sundeborg et al., Strother et al., Corn et al. and Maxim et al., to examine the quality of derivatized array substrates in the method of Okamoto et al., Rava et al. and Park et al. The motivation to do so is provided by Maxim et al., who state (col. 1, lines 43-56):

"The surface chemistry and the surface morphology of the microarray substrate is a factor that impacts the quality of microassay readings. The surfaces of both organic and inorganic substrates are typically modified by the deposition of a coating or a polymeric monolayer film to improve binding or attachment of biomolecules, promote adhesion and lubrication, modify the electrical and optical properties of the substrate surface, and create electroactive films suitable for various optical and electronic sensors and devices. Poor quality substrates result in low DNA binding efficiency, poor spot morphology, and fluorescent background that can be unacceptably high and nonuniform. Microarray substrates are susceptible to damage and degradation of the surface chemistry if they are not stored properly."

Therefore, as exemplified by the above references, contact angle measurements can be made to judge the degree of surface modification after every step of surface derivatization or to determine surface degradation after prolonged storage, in either case affording another level of quality control which is inexpensive to perform and prevents use of substrates with insufficient quality.

7. No claims are allowed.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Application/Control Number: 10/519,813

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July 25, 2009